Loo, Ti Li 1998

Dr. Ti Li Loo Oral History 1998

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National Cancer Institute History Project

Interview with Dr. Ti Li Loo

June 9, 1998

Interviewer: Gretchen Case

History Associates, Inc., Rockville, MD

GC: If you would just say your name for the tape recorder.

TL: My name is Ti Li Loo.

GC: Okay. This is Gretchen Case of HAI. I am interviewing Dr. Ti Li Loo. Today is June 9, 1998, and it is about ten o'clock. Okay. Should I just start by asking you questions?

TL: Sure, sure.

GC: Okay. I usually start by asking about your education and how you came to the NCI, so where you started from and how you got to the NCI.

TL: Actually I went to, my college education was in China, at a university. The name was Tsing Hua University, which was located in Beijing. Tsing Hua was quite famous. We had achieved three or four Nobel Laureates. The school was founded by the Boxer Indemnity Fund. That is, in 1900, I think, there was a war between eight powers, including the U.S., and the Chinese imperial government, and as a result of the war, China was compelled to pay indemnities to these eight powers. The U.S., under President Theodore Roosevelt, then decided to return the money to China and founded a university, called the Tsing Hua University, which is reputed to be the Harvard of China. And I went there.

I was trying to study medicine the first year. The War broke out after the second year and we moved; we evacuated from Beijing and went to Changsha and finally Kunming. Tsing Hua became associated with two other universities and was called Southwestern Associated University. I graduated from there in 1940. In 1942 I got a scholarship to study in Oxford, and I went there in 1943, at Magdalen College of Oxford University. I spent four years there to study chemistry and pharmacology. And then I went over to the U.S. Initially it was to study medicine but it ended up I was doing a postdoctoral fellowship. The first job was at the University of Maryland, then I moved to Cincinnati and worked with Dr. L. H. Schmidt, who was the Director of the Christ Hospital Medical Research Institute.

After three or four years I was recruited by Dr. Gordon Zubrod to join the staff of the NCI. That was in 1955 after I became an American citizen—during the Korean War I had a rough time in this country, because I wasn't allowed to go home and also I was not allowed to work, because I wasn't a citizen. But through the influence of Senator Howard Taft I was made an American citizen at the end of 1954, shortly after Christmas, I remember. Then in 1955 I was recruited by Dr. Zubrod, who was an exceedingly impressive, fine physician, scientist, and administrator. He wanted me to work on the pharmacology of anticancer drugs. At the time my colleagues included Dr. David Rall, Dr. Paul Condit, Dr. Jack Davidson, and Dr. Marion Freeman. Later on Dr. Zubrod was made the Clinical Director, in addition to being the Chief of the Medicine Branch, and the Pharmacology Laboratory was headed by Dr. David Rall. Then the clinical side of the medical branch was taken over by Dr. Emil Frei (who is called Tom) and assisted by Dr. Emil Freireich (who was called J). They were the intellectual twins.

GC: Were they called the intellectual twins, or is that just how you looked at them?

TL: Yes, because constantly they were paged; you would hear Dr. Frei, Dr. Emil Frei, Dr. Freireich, Dr. Emil Freireich. [Laughs] They were the twins. I worked there until 1965, when Dr. Frei decided to join the University of Texas M. D. Anderson Cancer Center. He was recruited by another very famous and energetic leader, Dr. Lee Clark. So, Dr. Frei asked Dr. Freireich and a few others, let me see now, Myron Karon, Dr. Myron Karon, Dr. Gerry Bodey, Dr. Ed Gehan, and myself to move from the NCI to M. D. Anderson. And I worked there until 1965. I retired in 1965 and returned to the Washington area and since that time I have been on the faculty of George Washington University Medical Center Pharmacology Department. I officially retired a second time in 1993, but I am still, my name is still on the faculty list of the Pharmacology Department at GWU.

GC: Do you still teach or research down there at all?

TL: Not any more. No. I had my last grant from the NIAID from 1990 to 1995, I think. All the dates are iffy, because I can't remember the exact dates.

GC: Okay. Well, the dates I can check up on. That's fine. How did you know Dr. Zubrod? How did you come to know him?

TL: Well, he was a very close friend of Dr. Schmidt. When I was at the University of Maryland, my boss was the late Dr. Drake, D-r-a-k-e, Nathan Drake, and he is a close friend with Zubrod and Schmidt, Dr. Schmidt. They all worked together on the malaria project during the war.

GC: Okay.

TL: And then Dr. Schmidt offered me a permanent job as a research associate at the Christ Hospital Medical Institute. My wife expressed a desire to move back to Washington, because she was brought up in the Washington area; her father was a diplomat, a Chinese diplomat. And since I became a citizen, I could work for the U.S. government. So, I was interviewed by Dr. Zubrod, who was closely associated with Schmidt. They were all very good friends. Dr. Shannon, of course, was the U.S. chief of the malaria research project.

GC: That was Dr. James Shannon?

TL: Yes. He died about two years ago.

GC: That's right. Now, when Dr. Zubrod asked you to come to the NCI, did he ask you to come for a specific project, or did he ask you just to come work for him and then . . .

TL: Well, yes and no. Not a specific project, but to work more or less in the area of cancer chemotherapy, to study the pharmacology, which involved the disposition, the metabolism, and the mechanism of action of anticancer agents. That's a broad, broad area. However, I'm allowed to choose whatever drug I wanted to study. He was a very broadly minded man.

GC: So, what was your first project? What did you choose to work on?

TL: First I worked on some thiopurines related to 6-mercaptopurine. Then the next one was on methotrexate, which is a very important drug even today.

GC: Was that with Dr. Hertz?

TL: No. That's Dr. Li. I was working on the basic science side. The clinic side was Dr. Li, Min Chiu Li, who died, unfortunately, of a heart attack about twenty years ago.

GC: So who did you work most closely with on these projects?

TL: Well, in the beginning I was with Dr. Zubrod, who was the Chief of the Medicine Branch. Then later on he was the Clinic director. The Pharmacology laboratory was taken over then, first was Dr. Condit and then succeeded by Dr. David Rall.

GC: Did you work on your own, or would you have a staff of lab assistants?

TL: I had technicians, and later on I had two junior associates, recruited by me. One was Dr. Oliverio, Vince Oliverio.

GC: Oh. I am going to try to interview him, too.

TL: Oh, yes. He is a *very* intelligent fellow. The other one was Dick, Richard Adamson. He is an amazing man. He got his Ph.D. when he was twenty-two.

GC: Twenty-two?

TL: Yes. He graduated from college at eighteen. He was one of the whiz kids.

GC: I guess so.

TL: Yes. We had quite a few whiz kids during the time when I was there. There were two very important things that fundamentally affected the NCI. One was—it was during the Vietnam War era, in that era—so, a lot of the scientists and physicians who didn't want to fight the War; they joined a uniformed service, the Public Health Service (PHS), and were commissioned PAs, officers with their own uniforms and ranks and so on. Some of these people were extremely bright, for example, Frei, Freireich, Dave Rall, and Adamson. They later on turned out to be great leaders in the area of biomedical research, particularly in cancer research. One important thing: the time was right for these people to get together under the leadership of Dr. Zubrod.

The second thing is the Cancer Act passed in Congress and all of a sudden we had a lot of money to spend. Dr. Zubrod took full advantage of this in developing the world-famous area of cancer chemotherapeutic research. Although an unassuming man, the fact is that without him there was no modern cancer chemotherapy. He was instrumental in integrating the clinical with basic research in cancer chemotherapy and made chemotherapy into a respectable modality of cancer treatment.

So, a lot of credit must be given to Dr. Zubrod, who is, as I said, one of the founding fathers of modern cancer chemotherapy. He is a scientist and physician and administrator, and a great leader. In the clinical side, of course, Frei and especially Freireich. In the basic sciences, Dr. Rall and Dr. Adamson and Dr. Oliverio. And then later on, the younger generation was Dr. Bruce Chabner and Dr.Vince DeVita. Dr. Oliverio was Vince DeVita's mentor. He trained him in the laboratory.

GC: Oh, I did not know that. I have interviewed Dr. DeVita, too.

TL: Oh, yes. He was, later on, of course, the NCI Director. Also he is a graduate of GW Medical School, our medical school.

GC: Right. That's right. You mentioned that Dr. Zubrod—you're right, he's very unassuming; he doesn't take as much credit as he should—that he really changed the way chemotherapy was perceived as being a modality that was worth something.

TL: Yes.

GC: How was it perceived before NCI started working [on chemotherapy]? Or did it even exist?

TL: Before there was no scientific basis. It has a haphazard kind of study. The first real study was by Dr. Gilman and Dr. Goodman, who noticed that people gassed by mustard gas had a tremendous leukopenia. Their white cells were wiped out. So he thought maybe in that case it would be interesting to treat leukemia patients with mustard gas. Of course, later on that developed into nitrogen mustard, which was a nitrogen analog of mustard gas.

GC: Yes. Actually, one of my relatives was treated with that treatment.

TL: Oh.

GC: It's an older one. They don't use it any more, do they?

TL: They still use some sort of mustard derivative, yes.

GC: Oh, they do? When did you begin working with Dr. Frei and Dr. Freireich?

TL: That's during the time when I was working with Dr. Zubrod. Yes. I was in the basic science arm and they were in the clinical arm. Another thing Dr. Zubrod did was to incorporate, to make the basic scientists and the clinicians work together as a whole. MDs and PhDs traditionally have sort of a rivalry. The MDs think the basic scientists are just "way out" and know nothing about patients, and the scientists, the PhDs, think the MDs are just pill-pushers. But under Dr. Zubrod, he could make them integrate into a very harmonious entity. They worked together on the same problem. So, that's another thing: You must give, people must give, a great deal of credit to Dr. Zubrod, where he can, as a leader, to make this working together as one unit: A unified concept of cancer chemotherapy. That was really wonderful.

GC: How did he do that? What did he do that helped that?

TL: He is a physician, but he did pharmacology research with Dr. E. K. Marshall, who was the Department Chairman of Pharmacology at Hopkins. Dr. Marshall was also a marvelous man. He started as a professor of physiology. He's a physician, but spent a lot of time working in the laboratory. In the beginning he was a physiologist and Hopkins decided to have a department of pharmacology and they started to recruit. And look who they recruited—they recruited Dr. Marshall, who was a professor of physiology. And then Dr. Zubrod had a keen interest in pharmacology studies, so he went there and worked as a fellow with Dr. Marshall and learned the basic lab techniques in the area of drugs. That's how Dr. Zubrod started to incorporate basic science into clinical medicine.

GC: Because he had experience with both sides of the work?

TL: Yes, yes.

GC: On a daily basis did he do anything to kind of keep people working together? Did he have meetings?

TL: He was working in the laboratory, in addition to seeing patients at Hopkins. But he went to St. Louis as a professor of medicine and pharmacology, I believe. You have to ask him. He wrote a book. Have you seen the book?

GC: Yes.

TL: He gave you a copy?

GC: Yes. *The Stairway of Surprise*?

TL: Yes, yes.

GC: It's beautiful!

TL: Yes.

GC: It's really beautiful.

TL: So, you know a lot about his career at NCI.

GC: When you were at NCI, did you see patients as well as working in the lab?

TL: No. I'm not a physician. I'm a scientist.

GC: Okay. But you would never accompany the physicians or anything?

TL: Yes, I did.

GC: Oh, you did?

TL: I made rounds with Dr. Zubrod.

GC: Oh, you did?

TL: Yes. Even though I'm not a physician. It was very confusing, because I am also introduced as Dr. Loo, even though I'm not a physician. So, when I made rounds, they [the patients] would think I was a physician but I was careful to say I'm not a physician. I'm not clinically qualified. I'm a laboratory scientist.

GC: But you would go on rounds with Dr. Zubrod?

TL: Yes, yes.

GC: Did you get to know the patients at all?

TL: Some of them, yes.

GC: Do any stand out in your memory as ones that you remember clearly?

TL: Yes. There was a commander, a Navy commander called Commander White, I think. He had carcinoid tumor, I think. That is also a very interesting disease that is sometimes responsive to chemotherapy, carcinoid tumor. He had it in the small intestine, I think. Under Dr. Zubrod's leadership, Dr. Hertz and Dr. Li demonstrated the treatment of the trophoblastic tumors with methotrexate. That was a major step in the history of cancer chemotherapy, because before that the only thing was nitrogen mustard, and this shows that certain antimetabolites would work, too, even though in a limited fashion.

GC: Now, you said you worked on methotrexate as well?

TL: Yes.

GC: But your project was totally separate from Dr. Hertz and Dr. Li?

TL: We used his patients' material, and also we used patients for the clinical pharmacology studies. This was later done entirely under the direction of Dr. Oliverio and Dr. Ed Henderson.

GC: Ed Henderson. That's not a name I've heard yet.

TL: Ed Henderson, I guess he retired. He's now with the FDA.

GC: The FDA?

TL: Yes. They published this, too. Oliverio and Henderson published the first definitive study on the pharmacology of methotrexate in man.

GC: What was the Clinical Center like when you got there? It just opened in 1953, and then you got there about two years later.

TL: Yes. It was very active. Of course, it was a new concept. The most important part was the Heart Institute. They really worked very, very close together, the clinicians and scientists. They had the world's most leading, the most successful biochemical pharmacologists at the time under Dr. Brodie, B-r-o-d-i-e, Brodie. They call him Steve, even though Steve was not his real name. Also Dr. Udenfriend and, of course, a Nobel Laureate, Dr. [Julius] Axelrod. Dr. Zubrod just wanted to start the same kind of set-up as the Heart Institute, in having a group of scientists working closely with the clinicians at NCI, and he succeeded beautifully. You can say he was in the right place at the right time, because of the influx of all these very bright scientists and physicians into the NIH, and also because of the Cancer Act, which was very much supported by a lady called Mrs. Lasker.

GC: Mary Lasker?

TL: Yes.

GC: Sure. Did you ever meet her, or did you know her?

TL: I met her once, but she could hardly remember me. She would come in and review our progress, and Dr. Zubrod would make us present our major findings before her and before other visitors. And also in the Congress, of course, Lister Hill, I think, a senator, Senator Hill.

GC: He's from Pennsylvania, I think? *[editorial note: Lister Hill was a senator from Alabama]*

TL: I forgot where he was from. I remember very influential senators and congressmen, plus Mrs. Lasker, helped a lot in pushing the enactment of the Cancer Act, which would also benefit us, after we left NCI, with Dr. Frei as the leader, at M. D. Anderson, because all our studies were supported by the NCI, through the contract or grant mechanism.

GC: Okay. Even when you were at M. D. Anderson?

TL: Yes. We still were known as affiliated with NCI, because we worked very closely with our past colleagues, Drs. Oliverio and Adamson, and later on Johns, David Johns. You probably heard of him.

GC: Yes. So, you mentioned that there was a lot of money. When you needed laboratory equipment or resources or people or anything like that, was that easy to get or was it hard to get?

TL: Oh, quite easy!

GC: Really?

TL: We were fully supported, first at the NCI. Dr. Zubrod would put his whole weight behind it, so we had no problem getting equipment and [chemical /biological] agents and personnel. The only thing that was a problem was space, not enough space.

GC: Oh, really?

TL: Yes.

GC: And was your laboratory in the Clinical Center?

TL: Yes. In the first place, in the beginning, it was on the sixth floor, then we moved to the tenth floor. Dr. Zubrod's office was also on the tenth floor, as well as the Cancer Ward was on the tenth floor.

GC: So, you were on the same floor as the patients.

TL: Yes.

GC: And what about getting people? Was that ever a problem, getting people?

TL: Well, getting people, you have to go through the Civil Service, the usual government regulations. So, it was not as easy as when we moved to Texas [M. D. Anderson]. The caliber of the junior scientists, the technicians, if I may say so, was somewhat higher in Texas than at NIH. The reason is at NIH all the technicians were protected by Civil Service. It's impossible to fire them, if they're not competent. But you don't have to record that! Because I have high respect for the NCI and my colleagues there. I just feel my technicians and the research associates at M. D. Anderson were of somewhat higher caliber. They were really wonderful people: very competent, worked very hard. They virtually made me. Everything I have done is through their help; without their help it is not possible.

GC: That's fine. Now, you've mentioned that you had a couple of associates working for you, Dr. Oliverio. Were you allowed to choose them, or were they assigned to you?

TL: No. I recruited them.

GC: You recruited them?

TL: Yes. Now, Dr. Adamson was recruited by Dr. Rall, I think, and assigned to me. Let's see, who else? Those are the two major ones.

GC: What was the last name of that doctor?

TL: Well, Dr. Adamson and Dr. Oliverio.

GC: They were the only two. Okay.

TL: I recruited people like Dr. Kurt Kohn, who is also now a famous biochemical pharmacologist. He was most impressive. I hired him to work with me for half a year and I exhausted all the things I could teach him.

GC: Really.

TL: He was so fast and so much ahead of everyone. So I sent him to Harvard to do a Ph.D., and he returned with the Ph.D., and M.D. A fantastic man! That's one of the people I remember most clearly.

GC: It sounds like you had some amazing people to work with.

TL: Incredible! Incredible! Such great leaders! I was so fortunate, because I also was at the right place at the right time with the right people.

GC: When Dr. Zubrod asked you to come to the NCI, did you know what kind of place it was? Had you heard of it before? Did you know that it had a reputation?

TL: Yes. Mostly because of the Heart Institute, because of Dr. Brodie, Dr. Udenfriend, those famous people. Dr. Gillette, James, Jim Gillette. But when Dr. Zubrod said he wanted to have the same set-up at NCI, I felt this is really a wonderful opportunity. Who could possibly join the NIH and world-famous medical research institution and to be close to those leaders and be on the ground floor to build up something in the cancer chemotherapy area. Of course, in the beginning we were quite naive. We thought we could conquer cancer just like we could conquer malaria (today even malaria is resurging as one of the major health problems) because nobody at the time could realize the emergence of resistance. In this regard we must give a lot of credit to Dr. L. H. Schmidt, who studied the chemotherapy of malaria and was also a world-famous man. He was one of the first to demonstrate the resistance of certain malaria bugs to chemotherapy. And then, of course, now cancer is gradually yielding to the combined effort of chemotherapy and biotherapy. I think we have made major, really tremendous progress—especially the current people, the young investigators. They know so much. Compared with us they were so much well-trained and extremely intelligent and with such a broad vision. I think compared with them, I know they are just way ahead of our generation, in my view.

GC: But then the NCI was ahead of anything that had been done before, right?

TL: Oh, yes. The NCI—another important thing is they spent most of their money in extramural research. So the money was equally, evenly, distributed among many, many cancer centers, and where they had extraordinary talents, too, like M. D. Anderson and Sloan-Kettering Institute and Roswell Park. But they must not forget they were very generously and very intelligently supported by people sitting at NCI doing the administration: Dr. Zubrod, Dr. Oliverio, and Dr. Vince DeVita. They did a very excellent job in distributing the funds, to see that progress was made in every area. This is just as important as laboratory research.

GC: And when you were on the other end of that, when you went to M. D. Anderson and you were then receiving money from NCI, how was that? Did you still feel that connection to NCI?

TL: Yes, because we had to submit proposals to the NCI and go through the peer review, and also review by the NCI and, of course, by our former colleagues and supervisors. So, intellectually and scientifically, we were just very close together.

GC: And, of course, you still knew all the people that you had worked with for all those years?

TL: Yes. We had to recruit *de novo*, all anew, build a new set-up at M. D. Anderson. Under Dr. Freireich, especially, it had become another international center of cancer chemotherapy.

GC: Because basically your whole team, that whole team of people, went to M. D. Anderson, right?

TL: Part of them. Some of the important people didn't leave, like Dr. Carbone, Paul Carbone, Dr. Henderson, Dr. Oliverio. They stayed behind.

GC: Was it a hard decision to make, to leave the NCI?

TL: Yes. In some ways yes and in some ways no. Of course, we had made friends. Our children were reluctant to leave their friends and this area. My wife was brought up in the Washington area, so she was reluctant to go. But it was a tremendous adventure to go to Texas. To us it was a wild country, you know, the Wild West. It turned out to be quite an adventure. And credit must also be given to Dr. Clark, Dr. Lee Clark. He played a very major part in the cancer research both nationally and internationally, and nationally and locally at M. D. Anderson. He built M. D. Anderson Research Institute, the hospital institute. He made it into one of the biggest and the most important ones in the world.

GC: And it still is.

TL: Yes. He can be classified as a benevolent autocratic director with a Texas mentality and personality. Absolutely a lovable man. But his words go. He says this and you must do it Or else!

GC: Sounds very different from Dr. Zubrod.

TL: Ah, yes, yes. Dr. Zubrod was democratic.

GC: So how would Dr. Zubrod manage things on a day-to-day basis?

TL: He had to delegate his authorities. He had very capable help in the person of Dr. Nat, Nathaniel Berlin.

GC: I interviewed him, too.

TL: Yes.

GC: He's wonderful.

TL: Yes. He's a physician and a medical physicist with a Ph.D. And a lot of extraordinary talents were helping Zubrod, like Dave Rall, Adamson, and Oliverio, DeVita, George Canellos.

GC: Okay, I've heard that name.

TL: Bruce Chabner.

GC: Now, can you tell me about Grand Rounds, what were Grand Rounds?

TL: Oh, Grand Rounds were the important occasion for integrating science with clinical medicine, because we were all encouraged to attend them and we did attend. I learned clinical management of cancer mostly through attending the Grand Rounds, headed by Dr. Zubrod and Dr. Frei and Dr. Freireich. They would present different subjects. For example, they were talking about the trophoblastic cancer and Dr. Li and Dr. Hertz would present, and the laboratory scientists at the time were Condit and Marion Freeman, who would present their studies of the disposition of methotrexate, how the blood levels, the CSF [central nervous system] levels relate to the clinical response—that kind of approach. And I would present what happened in the body, how it was metabolized and so on.

GC: So everybody got to hear the other side.

TL: Yes, yes.

GC: The other end of what was going on.

TL: Yes, yes.

GC: And how often did Grand Rounds occur?

TL: Every week.

GC: Every week?

TL: Every week would be presented some kind, some different subjects, different studies, ongoing studies, and some major, major problems indicated in the laboratory and so on. This tradition was carried on at M. D. Anderson.

GC: At M. D. Anderson?

TL: Yes. Especially under Dr. Freireich, who was very effective in integrating science with medicine.

GC: And that was something he had learned at the NCI?

TL: Yes. He learned a lot of things at NCI and did the same thing at M. D. Anderson. They recruited fellows and they were required to first serve a year on the wards, and then one year in the laboratory. So they know how laboratory research is conducted. They pick their own mentor and spend a year or two in the laboratory, in the same place, the same time. Dr. Freireich carried on the same tradition. So our physicians are different from the traditional ones: They know something about basic research. Some of them even spent time actually working in the laboratory.

GC: Just so they would have both sides of that [work]?

TL: I had more than ten M.D.'s in my laboratory, from various countries, at M. D. Anderson.

GC: So you said you had ten M.D.'s in your laboratory.

TL: More than ten M.D.;s and, of course, several Ph.D.'s from all over the world, mostly from China, Japan, and Germany.

GC: Yes. Was that unusual to have so many international people?

TL: No, no. It was quite common at M. D. Anderson. Because Dr. Freireich was world famous, he attracted many, many visitors and visiting scientists from all over the world, even today.

GC: Yes. Now, I've heard a lot of different versions on how Dr. Frei and Dr. Freireich and your whole team, when the combination chemotherapy was started, the medical establishment at large was not sure this was a good idea, and there was some resistance at first.

TL: Yes.

GC: Did you find that to be true?

TL: Very true. When I was interviewed by M. D. Anderson staff, I still remember what one of the leading physicians told me. He said, "You are wasting your time studying cancer chemotherapy, because it just poisons and kills the patient and is not doing any good," or something to that effect. That was in 1965. Dr. Zubrod and Dr. Frei and Dr. Freireich showed cancer chemotherapy was effective in certain types of cancer, even though we realized it wasn't universally successful in major types of cancer like lung cancer, breast cancer at the time. Today, of course, it's different. Even lung cancer and especially breast cancer in certain cases is treatable with chemotherapy. So at the time the established physicians, even at M. D. Anderson, were not, I wouldn't say hostile, but certainly were not very impressed by our approach that cancer chemotherapy plays a major part as a modality of treatment.

GC: Did anyone ever question your work as a part of this?

TL: No, no, no. They were very respectable. They respected the scientists more than they respected the physicians, especially because there were conflicts of interest, because they think their approach was the traditional way, and these young guys from the NCI came in and wanted to do something new that in their view was just a waste of time.

GC: Did Dr. Zubrod have to, what was Dr. Zubrod's position on all that? Did he just let them do whatever they wanted to do, or did he try to . . .

TL: No, he was the leader of the cancer chemotherapists. Of course, he was also an extremely effective administrator and a total gentleman. He never offended anybody using abusive language. That's why people respected him and would accept his judgment and his opinion. Dr. Freireich was—he is one of the most innovative clinical scientists of this century and remains one of the leaders in cancer chemotherapy, but he minces no words in expressing his opinion.

GC: That's true. And what about Dr. Frei? What kind of person was he when you worked with him?

TL: Dr. Frei is a marvelous man in that he has a very good general concept of all branches of medicine and of science. He is uniquely qualified in leading a group of scientists and physicians, because he makes you feel whatever you are doing is the most important thing in the world.

GC: Oh, really.

TL: He injects enthusiasm in every individual, so they are all loyal to him, especially Dr. Freireich, who was so loyal to Frei.

GC: They made quite a team.

TL: Freireich, of course, is the genius behind most of the innovative approaches to cancer chemotherapy. He was an iconoclast. He would break all the existing rules and concepts, for example, in leukopheresis, transfusion of platelets, and combination chemotherapy. Yesterday I was watching PBS on cancer research. They also talked about randomized clinical trial. He was, he and Dr. Gehan, were the first ones to say in certain cases you do not need randomization. In fact, randomization is unethical, because you know this patient, this cancer patient is going to die if you don't treat him, and you give him a placebo . . . Dr. Frei would say, "There's murder!"

GC: I can see that. I can see him saying that.

TL: He knows that normal randomization and historical control has a limit. He knows very well. He is a genius. But he says evaluating anticancer drugs is not like evaluating a drug for headache. You do not have to go through so many red tapes and rules. You should expedite the approval of a drug for clinical trial; this concept was later practiced by Dr. David Kessler, Dr. Kessler of the FDA, and nowadays the approval of anticancer drugs is so much speedier than before. It was also because Dr. Freireich was fighting for it.

GC: He didn't tell me about that.

TL: Oh, he was majorly responsible for the modern concept of the clinical trial, and the speedy approval by the FDA was entirely stimulated by him. He staked his career to fight for his positions. And, you know, Dr. Freireich, he's a flamboyant man.

GC: He is?

TL: We had a colleague, a junior colleague with me, an assistant professor under my supervision, who was diagnosed with cancer, with carcinoid, in fact. He was home and his physician told him there's no hope: just stay home and get ready for the inevitable. So, a friend of mine, another colleague of this cancer patient, went to see him in Florida, and he found he was very sick. So this friend called Dr. Freireich and said, "Dr. So and So is very sick and desperately needs help. His physicians say death is the immediate outcome." So Dr. Freireich flew there, gave him an examination, ordered an ambulance, and ordered a private Lear jet to fly him from Florida back to M. D. Anderson, and paid with his American Express card for the flight, of the several thousand dollars of airplane rental and the ambulance. All the time he was afraid M. D. Anderson wasn't going to reimburse him, but to him the patient's life is far more important than several thousand dollars, maybe tens of thousands of dollars. That's Dr. Freireich. His patients were the most important, research next. His patient's welfare is the most important thing in the world, then his research.

GC: That's amazing.

TL: Yes. So, anybody who says Dr. Freireich is hard to get along with and is difficult, I would say, wait until you know him well. Just watch his patients and ask his patients, "Is he a good doctor or not?" They would agree he is probably one of the best doctors in the world.

GC: It sounds like you were very loyal to him as well.

TL: He is one of my dearest friends, because he is so honest, so caring, so kind. It is probably to disguise his kindness, his gentleness, so he has a rough front. He puts up a front that's to scare people. But he is *really* nice. A most broadly trained man, he knows so much. Are you a scientist, in addition to being a writer and historian?

GC: Because I am a historian of science, I know a lot about science, but I wouldn't say I am a scientist. My father and my sister are both scientists, though, so I come out of that. My father is a chemist and my sister is a botanist. So, I grew up with science, but, no, I can't claim to have a degree in science.

TL: Yes. It doesn't matter. If you know as much science, you are a scientist.

GC: That's a good way to put it.

TL: So, science of history, that's very good. You know, my son-in-law is a scientist-writer.

GC: Oh, really?

TL: He works for *Business Week* as a scientist. His name is John Carey.

GC: John Carey.

TL: You may have read him.

GC: I am going to look for him.

TL: He is a writer.

GC: Yes, it's very interesting.

TL: A Yale graduate. He knows a lot of scientists, the science and also scientists, and he writes very well. He is an extremely intelligent fellow.

GC: It's amazing how much I've learned from talking to people like you about cancer research and about science. I've learned so much doing these interviews.

TL: Well, I'm sure you didn't learn much from me, but I'm sure you were impressed by Dr. Zubrod and Freireich, Frei. Frei is also very flamboyant.

GC: Is he?

TL: He's very broad [broadly trained]. He's a very friendly man.

GC: He's up in Boston now.

TL: Yes. Even though he's retired, he still works very hard.

GC: Yes. He still goes into his office?

TL: Freireich is not retired. Neither officially or unofficially. He is still working.

GC: You mentioned at one point that Mary Lasker and some of the senators were very supportive of the Cancer Act and the Cancer Institute and all that. Did you ever feel like that was, I know some people expressed concern that politics were getting involved with science. Was that ever a concern?

TL: No, no, no, no. If there is any kind of interaction with politics with cancer research, it is all for the good.

GC: All for the good.

TL: Yes. Occasionally there are some politicians that push their pet project and pet drug, but through the convincing arguments of Dr. Zubrod, Dr. Freireich, Dr. DeVita, they would change their mind. Like they would push for Laetrile, antineoplastin, and things like that. Quack medicine. They were shot down by scientists and physicians in the most effective, gentle manner. Otherwise a lot of money would be wasted in the wrong direction.

GC: Mary Lasker, did she ever come down to the lab? You said you would present for her?

TL: No. They were in a different building, in a conference room like this, they would sit in there and Dr. Zubrod would say, "Ti Li Loo will now present what we have found," and I would make a short ten- to fifteen-minute presentation of what we were doing and what's the purpose of doing it.

GC: So it was a very formal kind of presentation.

TL: I would say more informal than formal.

GC: Oh, okay.

TL: Because we had to tone down, making the presentation intelligible to these great supporters of ours. They never interfered. Never. They always give you tremendous support and encouragement. Never say to you, "Ti Li Loo, why don't you study Laetrile?"

GC: That's good.

TL: Yes.

GC: Did you ever go down to Congress? Did you ever go down to testify?

TL: No, no, never. No, I don't rank, I don't rate. That's for people like Zubrod, DeVita, and Dave Rall.

GC: Now, you must have worked under Dr. [John R.] Heller and Dr. [Kenneth M.] Endicott as directors. Is that right?

TL: Yes. They were way above me. They were the directors, yes.

GC: Did you have any contact with them, or did you know them at all?

TL: Yes. Dr. Heller, Dr. Endicott called me to their office, to talk about something. I've forgotten. It was a long time ago. Yes, just a short five or ten minutes talk. They wanted me to go there and ask me some questions. Impressive people, very good.

GC: What was Dr. Heller like?

TL: Oh, I can't remember. It's so long ago. Also there was a Stu Sessoms.

GC: And who was he?

TL: He was somewhat of a boss for a while, but I'm not really sure about it now. At the time I was low down on the totem pole and people above, I'm not sure who they are and what they do and who is whose bosses. Only later, gradually, we realized the hierarchy.

GC: Yes. Did your division or did the NCI get a lot bigger during the time you were there? You were there ten years. Did it grow a lot while you were there?

TL: Yes. Oh, there was a tremendous growth. New divisions were forming, reorganization, reallocation. Everything was going on. It was a very fast expansion; so many hired, so many personnel. Unbelievable.

GC: And was that good changes or did it affect your research in any way?

TL: Well, I think it was inevitable. When you have so much money to spend to expand the scope of your research, you have to increase the personnel. But when you increase the personnel, the politics become so complex.

GC: Oh, you mean interoffice politics?

TL: Yes. The internal politics becomes so complex. So I would much prefer to go to a small place, or a smaller place, like M. D. Anderson. That was one of the inducements to go to Texas.

GC: That was one of your reasons to go?

TL: Yes. Of course, Dr. Frei was very persuasive.

GC: Was he?

TL: Yes.

GC: How so?

TL: Well, he thinks it's a tremendous opportunity. He is the big boss. He will be in charge of all the chemical research over there, and Dr. Freireich would be his right-hand man. That's really a big attraction, you know. People who were recruited from NCI to go there were all first-caliber, I mean, the leading expert in their field: Myron Karon, Gerry Bodey, Evan Hersh, Ed Gehan. That's the people I remember. There were some others.

GC: Was there a lot of work between the Institutes? Did the Cancer Institute collaborate with the Heart Institute, or NIAID, or any of the others while you were there?

TL: Some. Not as much as I would have hoped. For example, at the time the best cancer research done at NIH was by the Heart Institute.

GC: Oh, really?

TL: Because of the carcinoid tumor and the biochemical and pharmacology involved. Of course, I contested, because later on our group was making some major contributions. But at the time we joined the NIH, it was true, because they were studying carcinoids. Carcinoid produces certain cardiovascular problems, as you know. Tricuspid insufficiency, the flush in the face, and so on. So, also the patients excreted 5-hydroxy indolacetic acid. There is a very strange kind of biochemistry going on in the patients.

GC: I noticed, I was looking at, you started in the OADR at NCI? Do you remember what that was?

TL: NODR?

GC: OADR. I was looking in the old directories.

TL: Oh, yes, yes, yes. Office of the Associate Director of Research, Dr. [G. Burroughs] Mider.

GC: Oh, you worked with Dr. Mider?**TL:** Dr. Mider was Dr. Zubrod's boss, and this Sessoms was Mider's boss and colleague or something. NCI is constantly changing. Even today. You never knew who your boss was going to be.

GC: Really?

TL: Dr. Mider recruited Dr. Zubrod.

GC: Right.

TL: Because Dr. Shannon recommended Dr. Mider to give these young physicians research experience, because Dr. Zubrod studied malaria with Dr. Marshall, and in that group was Dr. Shannon, Dr. Brodie, and all those people.

GC: Yes. Okay. So that's what that was. But you were doing research at that time, right?

TL: Yes.

GC: Because I noticed you went from OADR to the medical branch of the Clinical Pharmacology and Experimental Therapeutics Section, and then Laboratory of Chemical Pharmacology. And I didn't know if that was just that the names of the sections were changing or if you were actually moving offices?

TL: No. Just the names changing.

GC: Okay, okay.

TL: I moved my lab twice, from the sixth floor to the tenth floor, but nothing else.

GC: Nothing else really changed.

TL: No. No. The same, well, there were different bosses rotating.

GC: So that was just the reorganization.

TL: Yes, yes.

GC: That's interesting.

TL: Yes. So long ago. I have to think about it. I think mostly that is correct.

GC: Okay. When you would get a new boss or a new reorganization or something like that, did that affect the work you were doing, or was that just kind of outside . . .

TL: Oh, some, yes, because you have to consider the supervisor's personality and their approach. Not everybody is Dr. Zubrod, who is easy, understanding, sympathetic, encouraging. Dr. Freireich for about twenty years was my boss and he was different from Dr. Zubrod. Nonetheless, I enjoyed the opportunity to work with him. But an entirely different approach.

GC: Right. When did you, now, you didn't do any cancer research before you came to the Cancer Institute. Is that right?

TL: Yes. I was doing malaria research, first when I was in graduate school in Oxford, and then at the University of Maryland, and then in Christ Hospital with Dr. Schmidt. It was all malaria research. At the time malaria was a very important problem when we were fighting in Southeast Asia, New Guinea and the Philippines, and various places. Malaria was so debilitating and sometimes fatal.

GC: So, when Dr. Zubrod called you and said, "I want you to come do cancer research," what did you think about that shift in research? What did you think about cancer research? Or what did you think about cancer?

TL: “I have to learn!” I had to learn from the ground floor. I had a teacher, Dr. Zubrod is my teacher, my mentor. So I learned everything about cancer from him and cancer as a disease. Actually cancer is more than a hundred diseases, and the treatment and chemotherapy, it was all taught informally by Dr. Zubrod, through the rounds and through his papers, very effective man.

GC: Did other people coming in to the Institute have that same kind of experience, where they didn't have the previous experience with cancer and then they came to the Institute and learned it?

TL: Most of them never had any experience. Dave Rall never had any experience with cancer research. Paul Condit was not in cancer research, even though he was a physician. Jack Davidson was the only one with experience in cancer research, in biochemistry of cancer drugs. You know him, don't you?

GC: Jack Davidson?

TL: Yes.

GC: I was hoping to interview him. He is not very well, though. He wasn't able to do an interview with me.

TL: No. If you talk to Dr. Oliverio, you've covered talking with Dr. Davidson. His work is very familiar to Dr. Oliverio.

GC: Oh, good. That's good to hear. Yes, I hope to catch him.

TL: I have high respect for Dr. Davidson.

GC: He did some very good research.

TL: *Very*, very good, very good. An amazing man. He is also highly specialized in radiochemistry.

GC: What was the best thing about working, about doing research, at the National Cancer Institute?

TL: The first was the colleagues. The caliber of your colleagues was so impressive, and you can really learn a lot from your colleagues. The second is that the resources are quite ample, other than the space. You are not limited by equipment, by drugs, animals, and you had plenty of supplies. Third is the reputation of the NIH as a major international biomedical research center. So, the place, the personnel, and the resources. There was a time when I was there you would never have to worry about your budget. Nowadays you have to, because you have external review. In my time the review was there but very informal. There was no site visit. The reviewers would come and you would just give a ten- or fifteen-minute presentation. Not as serious as at M. D. Anderson, which sometimes consumed two or three days, where you have to take care of site visitors. We had to rehearse internally and then, of course, above all you have to work terribly hard; otherwise, you don't get your papers published and you have no grants.

GC: Was it easy to get published, being from the NCI?

TL: No, no, no, no.

GC: No? It didn't make any difference?

TL: No, no. It was totally impartial peer review. If you don't have anything, nobody is going to accept it, whether you are from the NCI or from M. D. Anderson. It will be rejected outright. Sometimes even a very good paper would be rejected.

GC: Not what they wanted.

TL: No.

GC: How did the reputation help you? You said you really enjoyed the reputation of the Institute.

TL: Oh, yes, yes. Because when you go out for your meeting, you say you are from the NCI, the reaction from the audience is entirely different.

GC: Really.

TL: They show their respect. The same at M. D. Anderson.

GC: You said that all the resources were ample, except for space. Why was space such a problem?

TL: Well, as you can see, the clinical center was just built and we had one module, every senior investigator has one module that is about twice as big as this room. When you get going with the equipment and the technicians, it is very crowded. And usually you get involved in more than one project and you wish you had more than one module.

GC: So a module was maybe 25 feet by 35 feet? Something like that?

TL: Yes, something. The walls are moveable. You can tear down and remodel very easily. But the place is expanding, all the people are coming in. There constantly is a shortage of space. That's why later on they moved the administrative, extramural staff, away from the laboratories.

GC: Just so they could have . . .

TL: Now they're farmed out all over the place.

GC: Yes, they are in all different buildings now.

TL: Yes.

GC: Was there anything you did not like about working at the NCI? Were there any problems inherent to that place?

TL: Not really. The only thing is, when you get bigger, there is more internal politics and personalities to deal with, which I wished I didn't have to. Just concentrate on doing my work and not trying to make my boss happy and that sort of thing.

GC: I think that happens a lot of places.

TL: It's inevitable. When you have more than two people, there is politics because you always want to win the third man to you. That idea of constantly working harmoniously and no difference in your opinion, that's impossible.

GC: That's great. What was a typical day like for you? What time would you come in to work and what kind of activities would you do? Then when would you leave? How long would you be there?

TL: Oh. When I was working very hard, no problems bother me. I come in frequently about seven o'clock [a.m.]. First is getting things started. Second, at the time there was no reserve parking, so I could park in the front. And I seldom would leave before six o'clock [p.m.].

GC: That's a long day.

TL: Yes. This I carried to M. D. Anderson. I got there even earlier, I got in initially at six o'clock [a.m.] and worked until after six o'clock [p.m.], because it was very competitive for the department money at NCI. You don't get work done, you have nothing to publish and nothing to present, you have no record, and you get no grants, and you can't do your research. You know, the publish or perish principle.

GC: Oh, yes. It's the same in history.

TL: It's true today and was true and it will be true, because there is nothing else you can do. Research is not economical. It doesn't produce anything tangible that will be economically productive. A lot of research may not even help the patient directly. Some of it, we hope, will. Very often the research turns out to be a failure. I studied more than fifty drugs. Probably most of them weren't active in the clinic. Useless. No more than five or ten drugs I studied turned out to be good. A couple of them are good today. Methotrexate is one. We spent a lot of time wasted. But who can tell? You cannot predict just from your animal studies, preclinical studies that this drug is going to be useful or useless clinically. You can't predict.

GC: Right. Did you feel like there was a good balance between basic research and clinical research?

TL: Yes.

GC: Or applied research?

TL: Yes, yes. Yes, I think under the leadership of Dr. Zubrod and Dr. Freireich, yes. We had very good balance and good support. We made a lot of progress that can be used in the clinical direction immediately.

GC: You have answered my questions so well. I just wanted to check and make sure I didn't miss anything. What was the atmosphere like in your laboratory? What was the general atmosphere? How did people work together?

TL: Very well, very easy. There were no, except in very few cases, no strong personalities. The technicians, most of them were very competent, worked hard, except I feel that they were not as dedicated as at M. D. Anderson, because they are more or less bureaucrats protected by the Civil Service system. Come in 8 [a.m.] to 5 [p.m.], 8 to 5. If you ask them to stay late or come in early, they usually agree reluctantly and, of course, they would take comp time later. Not as devoted as at M. D. Anderson. You asked them to do something, they used to do the job as necessary, to stay late or to come in early and do it. And they would not count the pennies and say, "I took a half an hour off now because I was in a half an hour early some time." But on the whole they were dedicated. Most of them were competent and not very many strange personalities to deal with.

GC: That's good. Were there teams of people working on certain projects, or did people kind of move between projects in and out?

TL: Usually the senior investigator will pick several projects. When I was working on, for example, methotrexate, I also worked on thiopurines, and also I worked on some other drugs at the same time. When you were stuck on one area, you go and jump in another one. You put your emphasis on that. You can't always count on that your work on this one is going to be a success. Sometimes you get stuck and you may not have anything to publish for several years. This philosophy I learned in America. When I was in Britain, it's not so critical, that publish or perish. Later on, of course, you learn quite a bit in the system and you gradually become Americanized. Nowadays in Oxford, Cambridge, it's the same thing—if you don't publish, you don't survive. Well, there's no record! You have to think about what other record do you have? You say, "This man is very productive, made a lot of progress." But it's all in his head! That's no good. You can't present it. That is, you have to get it in print and everybody agrees that this is a good piece of work. So, publish or perish is necessary, but this should not be pushed too far and say, unless you publish one paper a year you will never be promoted. That kind of attitude should not be adopted. On the other hand, Dr. Schmidt, in his later years he didn't publish much.

GC: He didn't.

TL: He has loads, *loads*, tons of data, but never published! Later, through the gentle persuasion of Dr. Zubrod and Dr. Marshall, he had several thick volumes published in the Cancer Chemotherapy Reports, which you can find in the library. But a lot of things are buried, because his work got so much ahead of his publications, he couldn't ever catch up. That's one of the mistakes he made.

GC: So he just never was able to analyze all that data.

TL: He did his analysis. He didn't publish. If you ask him, he would give you the data, but that is not in print, so nobody can refer to it.

GC: Wow. So, if you had several projects going on at one time, your technicians would also shift, according to what you were stressing at that time?

TL: Yes, yes. Depends on my own strategy at the time, "Let's all work on this . . ." and so on.

GC: This is tape two, with Gretchen Case interviewing Dr. Loo on June 9, 1998. Do you know—this is a question I asked Dr. Rall, too, and he wasn't sure—do you know if the Laboratory of Pharmacology came out of one of the, the NCI was formed from a division of NIH downtown that was called the Laboratory of Pharmacology and then the Office of Cancer Investigations at Harvard, and those two labs came together to form the NCI in the late 1930s, in 1939. Do you know if the Laboratory of Pharmacology that you worked in was part of one of those original divisions, or if it was created later?

TL: No, no. It was created entirely by Dr. Zubrod, *de novo* from the beginning. It recruited the staff in certain directions. It was entirely Dr. Zubrod.

GC: Okay.

TL: Before that there was no Laboratory of Pharmacology as such.

GC: Okay.

TL: There were people studying experimental cancer chemotherapy in laboratory animals, mostly mice and rats, for example, Dr. Abe Goldin, who died of cancer fifteen years ago. He was one of the major scientists who contributed from the basic science point of view to clinical cancer research. Unfortunately, you will not be able to interview him. He was a very important player in the field.

GC: Yes. His name has come up quite a bit.

TL: Yes. And then there was a doctor, I can't remember his name. Well, so many individuals who later took on major responsibility at the NCI. I'm stuck with names.

GC: That's okay. Most of them I can look up, so don't worry about names or dates or anything. This is a kind of tangential question, but when you worked, you used, I assume, rats and mice and different animals. Did you have, did each lab have, their own supply of animals, or was there a central animal room or animal facility?

TL: At NIH there was a central animal supply, away from Building 10. They were in a very fine building. It was very well managed. We had plenty of, at that time, of course, the animal rights people were not so active, so we had monkeys, dogs, rats, and mice. This research was mostly done with mice and then rats, then dogs, I think, and monkeys.

GC: But if you needed animals, you didn't have to order out to a supplier?

TL: No, no, no. We would just go to the animal quarters. Of course, you had to give them notice, on a certain day, at a certain time you need this kind of animal, and so on. They were housed, however, the rodents were housed in Building 10. The dogs and the monkeys were housed separately, entirely separate, and the stock animals, the rodents mostly were housed separate.

GC: Yes. That's probably good.

TL: Yes. Nowadays I think they moved away.

GC: What was your favorite project, or the way that you feel you contributed the most to the NCI, what do you remember most about being at the Institute?

TL: At NCI, the thing I remember most is methotrexate.

GC: Methotrexate?

TL: Yes. The other thing is I was also trying to show that, at the time they had a drug called methyl-GAG.

GC: Methyl-GAG?

TL: Yes. Methyl-GAG, G-A-G—what G-A-G stands for I can't remember—methyl-GAG, which was used in leukemia and very effective. But it has very, very strong side effects so it is not used any more. And then there was a gentleman who published a paper that said, hydroxy-methyl-GAG, which is a certain experimental cancer agent which he said is better than methyl-GAG. This is a negative study, because I proved his hydroxy-methyl-GAG was methyl-GAG itself with a molecule of water.

GC: Oh, really.

TL: And then I made methyl-GAG myself and proved that the new methyl-GAG was no better than methyl-GAG. Let me correct it. I made the real hydroxy-methyl-GAG, which turned out to be no better than methyl-GAG. But I spent a long time, six months or so, and made it. The other study I initiated was the metabolism of cyclophosphamate, cyclophosphamate. I had a theory it was oxidation, at the time people were suspecting the drug was hydrolyzed *in vivo* to give you nitrogen mustard, and I said it isn't. I didn't have the solid experimental evidence, but based on my theory, I said it can't possibly be a hydrolytic process but an oxidative process. And then I tried to make the metabolite to prove I was right; that's the end of the study—I never made it and never proved it. It was up to somebody else in the laboratory to prove it was an oxidative process. But I was the first one to propose it was oxidation rather than hydrolysis.

GC: So even though you were the first one to propose it, no one ever acknowledged that.

TL: Yes. Because I just went to meetings and said, "I think this is an oxidation." First, you publish nothing and second you have no evidence, laboratory evidence of this, that's no study. I agree, that's no study.

GC: Now, with the hydroxy-methyl-GAG, when you disproved, when you proved that it was just methyl-GAG with a molecule of water of hydration, as you said, was that, did that, I don't know what the right word to use is, did that cause an upset or a . . .

TL: Yes, yes.

GC: Can you tell me about that?

TL: Yes. There was a Szent-Györgyi. Do you know Szent-Györgyi? He was a Nobel Laureate. He said—I can't remember exactly what he said—he said something like, "Cancer is caused by something that could also cure cancer at the same time if the molecules were switched around." He had that theory, that cancer drugs and carcinogenic compounds could be one and the same. With little structural modification, they become anticancer drugs, with little structural modification, become carcinogenic compounds. Which is interesting, but there is no proof. Then he cited, he said, for example, "Methyl-GAG cures cancer and hydroxy." No, he said, he said something like "Methyl-GAG . . ."

GC: Causes cancer?

TL: "Causes leukopenia; hydroxy-methyl-GAG doesn't." Something like that. Again, you'll have to go to check.

GC: Okay. I'll check that.

TL: So I said, "That's nonsense, because you didn't make hydroxymethyl-GAG. I've made it." So that was an argument with a Nobel Laureate. I said, "He cannot cite the story of methyl-GAG as an example, because hydroxymethyl-GAG has never been made until I made it."

GC: Now, was this an argument in print, or was this an argument, in fact, in person? Did you ever speak to . . . ?

TL: Yes, it was in *Science*. There was a letter to the editor.

GC: Oh. Wow.

TL: He published some kind of comment, “Even though your theory may be right, I don't believe it’s right.” But to cite methyl-GAG and hydroxy-methyl-GAG as supporting vidence of your theories is wrong, because nobody had hydroxy-methyl-GAG until I made it.

GC: That's quite a feat, to have an argument with a Nobel Laureate.

TL: Yes. Later on he had his final say, he said maybe I [Dr. Loo] never made it either. But I didn't want to keep on, because I had better training in synthetic chemistry, and I know I made it. I have the physical chemical evidence.

GC: Can you think of who else I should talk to from the NCI? I can tell you I talked to Dr. Frei and Dr. Freireich and Dr. Zubrod, and Dr. Rall and Dr. Berlin.

TL: Yes. And Oliverio, you're going to talk to.

GC: I will talk to Oliverio.

TL: And the other guy is Shepartz. Saul Shepartz.

GC: Saul Shepartz?

TL: Yes.

GC: Is he still, do you know where he is?

TL: No. He's retired, but he, in fact, he has a long history associated with the NCI, especially with the Division of Cancer Treatment. A very famous man, so you can, so there’s no chance you can miss him. Because he knows so many people, because he has spent so many years with the NCI.

GC: So he is one I should definitely talk to?

TL: Yes. As a basic scientist and administrator, not as a physician. [Jack] Davidson, if available, is very interesting to talk to, but [laughs] he might not even remember as much as I do.

GC: Okay. Yes, I told him I would check back with him after a while, so I'll do that.

TL: Dave Rall. Richard Adamson.

GC: Okay.

TL: He's in town.

GC: He's in town?

TL: Yes. He lives in Potomac. His telephone is probably in the book, I think.

GC: Okay, good. And he was one of your associates, right? Your clinical associates that worked for you?

TL: In the beginning he was an associate, but his star rose so fast. He became the Associate Director for Cancer Etiology and was acting as the NCI Director for several months, I think, when DeVita left.

GC: Is that right?! I was wondering who that was, because DeVita left and then someone didn't, Broder didn't come in right away.

TL: Yes.

GC: So that's who was in there?

TL: Yes.

GC: Okay.

TL: Richard Adamson.

GC: That's very interesting.

TL: The guy who got his Ph.D. at twenty-two, graduated from college at eighteen.

GC: Unbelievable.

TL: Yes.

GC: Unbelievable.

TL: We had a Ph.D., another Ph.D., at the time, also a whiz kid. I forgot his name, unfortunately. There's another one. And there were a lot of physicians that were there. Like Dr. Freireich, he got his M.D. at twenty-two.

GC: Dr. Freireich did, too?

TL: Didn't you know that?

GC: Well, I guess I never . . .

TL: He went to medical school at eighteen.

GC: I did know that. I did know that! You're right. Because we talked about that, being away from home at eighteen, for medical school. Oh, my goodness, I can't imagine.

TL: You didn't know he was such a genius.

GC: I did know. Everyone told me he was a genius, and then when I met him I figured it out. He's quite interesting.

TL: I have written a chapter on cancer chemotherapy with him. It was published two years ago. The data is probably . . . it is five years outdated. I will send you a copy of the book, the whole book.

GC: I would like that.

TL: It's called *Principles of Pharmacology*. The chapter on cancer chemotherapy was written by Freireich and me and dedicated to Zubrod. I will bring it to you one day as a souvenir.

GC: I would like that. I would love that. Have I missed anything?

TL: It's up to you.

GC: Okay. You've answered so many of my questions. I think I've gotten, had the virus cancer program started when you were there?

TL: Yes.

GC: Did you have any involvement in that?

TL: No, no.

GC: That was pretty separate, wasn't it?

TL: Yes. And the person who was famous there was Dick Rauscher.

GC: Right, right.

TL: And he became the only Ph.D. to head NCI.

GC: Right.

TL: He was very, very good.

GC: So you knew him?

TL: I knew him by casual acquaintance, not well. Dr. Zubrod and he worked together, of course, and Vince DeVita.

GC: Did it make a difference when the directors of NCI changed? Like when Heller left and Endicott came?

TL: No. Nothing to do with us.

GC: Nothing to do with you?

TL: No. Not from the division chief [levels of administration] down. Nothing to do with us. Only with the associate directors, division chiefs, and the big-shots.

GC: Yes. Okay. Were you at M. D. Anderson in the 1970s, when the National Cancer Act, the War on Cancer, was declared?

TL: Yes, yes, yes.

GC: What did you think about all that?

TL: Oh, I think it was a great idea, except people wrongly put too much hope on it. They think if you put a lot of money in, the cancer problem will be solved. It isn't as easy as that. Dr. Zubrod explained very clearly that cancer is more than a hundred diseases. We don't even know what really causes cancer. There are so many factors, etiological factors. They all cause cancer, but which one has caused this particular cancer in this particular patient? And we don't know the genetic defect at the time. So, people should be patient. The progress we are making today is just as predicted. That was a very major advance in the politics of cancer research, to give the scientists and physicians the money to push for it, even though at times the progress is so slow that the people become disheartened and start to criticize. Some of the criticism is really unjustifiable.

GC: Yes. I know when the Act was passed in 1971, and the War on Cancer was declared, and they said by 1976 we want to have cancer cured. What did scientists think of that at the time?

TL: I think it was overly optimistic. To set a time is wrong. Progress is made, especially in basic science, molecular biology, by leaps and bounds. All of this eventually will have a major impact on clinical cancer treatment. You don't know at this time how important a certain discovery really is, as the progress in immunology and molecular biology recently realized, you can see maybe that cancer is going to be cured in five years. Who knows?! Maybe we really have the magic bullet. It's hard to say. Nobody can, in his sane mind, predict, although I am very optimistic.

GC: And you're still very optimistic?

TL: Yes. Absolutely. I can't put a, give you a time, but I say there will be a cure for the disease. Just like AIDS.

GC: Really?

TL: Yes. In the beginning, when I was in AIDS research five years ago—I had a grant from the NIAID—I thought this will be no serious problem, that one virus causes the one disease. I didn't know the virus was so smart and changes so fast. It was the first time, not the first time, in fact, that I made a major mistake. I gave up major research because I think my knowledge of molecular biology is so rudimentary, I can never come up with a real major advance in the chemotherapy of AIDS. But it will be solved. The young people are so smart.

GC: Well, they've done so much already with the new . . .

TL: Unbelievable. They have a vaccine now.

GC: Yes.

TL: In clinical trial.

GC: Yes. It really is unbelievable.

TL: Any other questions?

GC: I think we mostly got it. Did you work, you talked a little bit about you worked from like 7:00 a.m. to 6:00 p.m. Did you work weekends sometimes, too, if you needed to?

TL: I worked much harder at M. D. Anderson, and at NIH the last few years I worked very hard. In the beginning my children were young, so I had to spend a lot of time, spare time, with them.

GC: Right.

TL: Which was absolutely necessary and really very enjoyable. Later on, when they were in high school, I could let them stay home by themselves, and with Dr. Freireich—he worked very hard, too, you know—we worked on Saturdays, yes, at least a half-day.

GC: On Saturdays.

TL: Yes. Dr. Freireich was a very inspiring man.

GC: It sounds like it.

TL: Oh, he's a delight to work with. Dr. Zubrod, of course, was an old-fashioned gentleman-scientist. Very just, very right, very polite. Most impressive.

GC: I was very impressed by him. I really enjoyed meeting him.

TL: Anything else?

GC: I think that's all. Do you have anything you'd like to add before I turn off the tape recorder?

TL: Now, if you have questions, you can always ask me over the phone again.

GC: Okay. Let me stop the tape.

TL: You have my phone number?

GC: Yes.

TL: Which is unlisted. But you have it.

GC: I got it from the [alumni] directory.

TL: Yes. In the book.

End of transcript